**REMARKS/ARGUMENTS**

Applicant's attorney wishes to thank Examiner Wortman for the courtesies extended during the interview of April 23, 2003.

Claims 19-33 currently appear in this application. The Office Action of March 19, 2003, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicants respectfully request favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

**New Matter**

The amendment filed February 27, 2003, is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure.

The specification has now been amended to correct an inadvertent typographical error.

**Claim Objections**

Claims 6, 13, 17 and 18 are objected to because of misspellings.

The present amendment replaces these claims and it is believed that the spelling errors have been corrected.

**Rejections under 35 U.S.C. 112**

Claims 3 and 4 are rejected under 35 U.S.C. 112, second paragraph, as filing to set forth the subject matter which applicants regard as their invention.

This rejection is respectfully traversed. The present amendment cancels claims 1-18 in favor of new claims 19-33. It is believed that these new claims more accurately define the invention for which patent protection is solicited.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection is respectfully traversed. It should be noted that paragraph 0019 of the specification as filed states that the TNF neutralizing compounds were found to reverse the clinical symptoms associated with hepatitis, including normalization of liver enzymes and decrease in serum viral levels. Submitted herewith is a declaration of Dr. Ashok Amin and Dr. Steven Abramson describing in more detail the treatment of patients described in paragraph 0019 in the specification. It should be noted in Table 1 that when patient 2

discontinued etanercept, the viral load increased significantly. For patient 3, the viral load decreased by a faction of 100. For patient 5, the viral load initially increased but later decreased substantially.

It should be noted that some patients did not have elevated liver enzymes prior to treatment, although patients with elevated liver enzymes treated with etanercept exhibited an improvement in this measurement of liver function. However, it is clear from the declaration that patients treated with a compound that neutralizes the effect of secreted TNF alpha showed improvement resulting from this treatment.

**Art Rejections**

Claims 1, 2, 7, 9 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by *The Merck Manual of Diagnosis and Therapy*, pages 384-386.

This rejection is respectfully traversed. Claims 1-18 have been cancelled in favor of new claims 19-33. These new claims recite neutralizing the effect of secreted TNF alpha, or reducing the viral load in a patient. There is nothing in *The Merck Manual* that teaches or suggests treating with an effective amount of a compound for neutralizing the effect of secreted TNF alpha or reducing the viral load in a patient, particularly since *The Merck Manual* said that results of

using interferon to treat hepatitis were relatively disappointing.

In support of the unexpected success of treating patients with viral hepatitis with a compound that neutralizes the effect of secreted TNF alpha, copies of the following articles are submitted herewith:

*Ann Rheum Dis* 2000; **59** (Suppl 1):i1-i2;

*Ann Rheum Dis* 2001; **60** (Suppl 3):i2-i5;

*Ann Rheum Dis* 2002; **61**i2-i7;

Zylberberg et al., *J Hepatol 1999* ***30(2):*** 185-191;(abstract only)

Peterson et al., *Arthritis Rheum* 2001 **44(suppl)**:S78 (abstract only)

Tilg et al., *J Hepatol* 2003 **38(4)** 19-25 (abstract only)

It will be noted from the consensus papers note that TNF blocking agents should not be started or should be discontinued when serious infections occur (2000, 2001, 2002). It is clear that a consensus of physicians as late as 2002 believed that TNF alpha blocking agents should not be used to treat patients with a serious infection. Hepatitis is, of course, a serious infection. Thus, there is no motivation to treat patients suffering from hepatitis with a TNF alpha blocking agents.

In view of the above, it is respectfully submitted that the claims are now in condition for

allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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